THE

SCIENTIFIC PROCEEDINGS

OF THE

ROYAL DUBLIN SOCIETY

VOL. 25 (N.S.)

No. 3. APRIL, 1949.

SULPHURIC ACID AS CATALYST IN ACYLATIONS WITH ACYL CHLORIDES.

BY J. G. BELTON, N. V. NOWLAN AND T. S. WHEELER.

DUBLIN :

PUBLISHED BY THE ROYAL DUBLIN SOCIETY,
BALL'S BRIDGE, DUBLIN

HODGES, FIGGIS, AND CO.
6 DAWSON STREET, DUBLIN.

WILLIAMS AND NORGATE,
36 GREAT RUSSELL STREET, LONDON, W.C.1.

1949.

Price: Three Shillings.

COMMONWEALTH MYCOLOGICAL INSTITUTE
20 MAY 1949

No. 3.

SULPHURIC ACID AS CATALYST IN ACYLATIONS WITH ACYL CHLORIDES.

By

J. G. BELTON, N. V. NOWLAN and T. S. WHEELER.

[Read February, 22. Published April 27, 1949].

A demand in this laboratory for phloracetophenone trimethyl ether (II ; Fig. 1) led to an examination of its production. Application of the normal Friedel-Crafts method to phloroglucinol trimethyl ether (I) gives unsatisfactory yields owing to the reactivity of the aromatic nucleus with three anionoid groups. (See 36). Friedländer and Schnell (21) claimed to have obtained in this way (II) contaminated with the 4 : 6-dimethyl ether (III), but Tutin and Caton (73) were unable to reproduce these results. Kostanecki and Tambor (44) employed the less active ferric chloride in place of aluminium chloride, obtaining an " excellent " yield ; Nencki (51) gives this yield as 100%, Tutin and Caton (73) say it was good, while Freudenberg (18) gives a figure of nearly 90%. On the other hand, Cullinane, Algar, and Ryan (10), found the use of ferric chloride troublesome (1), and Gulati and Venkataraman (30) preferred to employ aluminium chloride and to control the reaction by working at −5° to −10° ; their yield was 61%. It has now been found that replacement of aluminium chloride by the less active electrophilic catalyst, sulphuric acid, enables (II) to be prepared from (I) in quantitative yield.

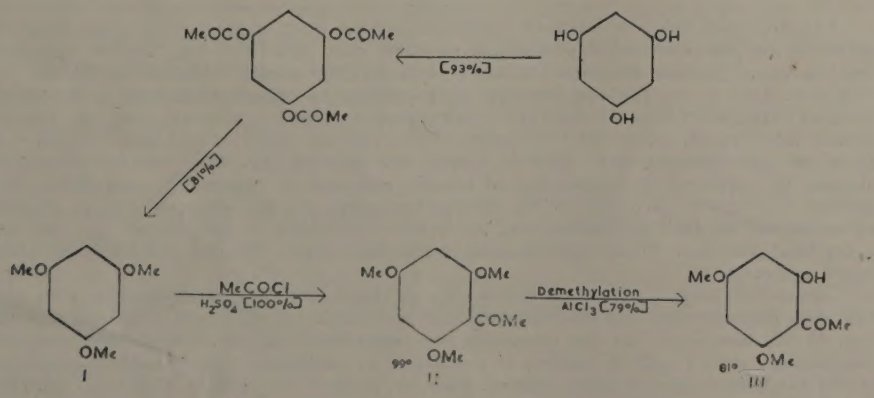


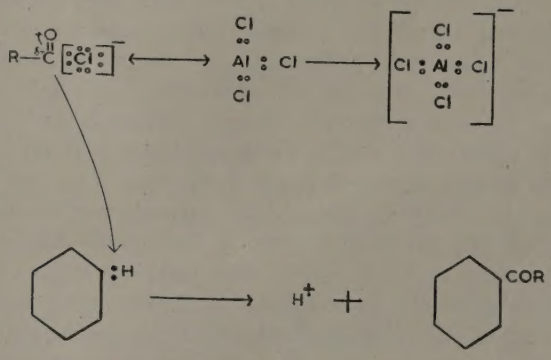
Fig. 1.

Previous Work with Sulphuric Acid.

Although the use of sulphuric acid and an anhydride as an acylating reagent is well known (6, 31, 38, 39, 40, 43, 64, 65, 66), few instances have been found of the use of this acid with an acid chloride. Israelstam (38) obtained satisfactory yields of resaceto- and resdiaceto-phenones from resorcinol, acetyl chloride, and sulphuric acid.* In this connection it may be mentioned that Cox (9) states that resorcinol can be acylated in the nucleus with an acid chloride without addition of a catalyst (cf. 48, 52). Hartough and Kosak (31) in describing the acylation of thiophene and furan with strong inorganic oxyacids and acid anhydrides mention that acyl halides can be used. The anionoid activity of these nuclei corresponds to calculated figures for electron distribution (58). It may also be mentioned that Gottesman (27) employed acetyl chloride with a trace of sulphuric acid for cyclizations involving dehydration.

Nature of Catalytic Action.

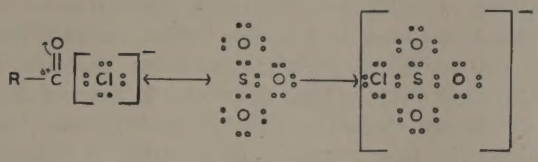
The catalytic action of aluminium chloride is probably to be referred to the electron deficiency of the aluminium atom (see 47 p. 115 ; 7, 13, 16, 17, 46, 56, 57, 72), which removes chlorion from the acyl chloride to form an acyl cation :—



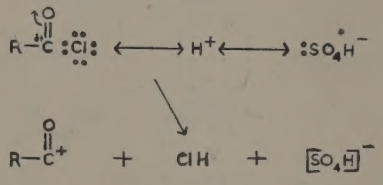
* In discussing the production of phloracetophenone (70% yield) by the action of acetic anhydride on phloroglucinol in presence of sulphuric acid, Israelstam and Stephen (40) state that the m.p. of phloracetophenone is 213-4°, and that the product obtained by Hoesch (36) with m.p. 218° is the ketimine sulphate corresponding to phloracetophenone. This seems doubtful, since, apart from the analytical results given by Hoesch (36), Gulati, Seth, and Venkataraman (29 ; cf. 28, 30, 60) used hydrogen chloride and not sulphuric acid, and obtained m.p. 218-9° for phloracetophenone. Further, Leuchs and Sperling (45), who prepared phloracetophenone by a method other than that of Hoesch, obtained the higher m.p., and Heller, who initially (34) reported m.p. 209-10° for phloracetophenone prepared from phlordi- or phlortriacetophenone, obtained the higher m.p. on further purification of his product (35 ; see also 5, 61, 68). The m.p. of phloracetophenone is also discussed by Howells and Little (37), who record 218-218.5°.

Again, Israelstam (38 ; cf. 39) claimed the production of phlordiacetophenone with m.p. 153° from phloroglucinol and acetic anhydride in presence of sulphuric acid, indicating that the m.p. of this compound had not previously been recorded. (See 51). The claim needs re-examination, since C and H analysis is insufficient to distinguish between phlorglucinol and any of the hydroxyacetophenones derived from it ; all have the formula $(C_2H_2O)_n$. Göschke and Tambor (26) and Heller (33, 34) give the m.p. of phlordiacetophenone as 168-70° and of phlortriacetophenone as 156°.

The electrophilic action of sulphuric acid may be due to the presence of the canonical form of sulphur trioxide in which the sulphur atom is electrophilic (47 ; p. 109).



It is possible, however, that chlorion is removed from the acyl chloride by a proton from the acid :—



DISCUSSION OF RESULTS.

In view of the satisfactory results with (I), the work was extended to phenyl and naphthyl ethers using acetyl and cinnamoyl chlorides. A survey of the results set out in Figs. 1–4 and in the experimental section shows that the sulphuric acid-acyl chloride method of acylation is of limited application, and that in general aluminium chloride gives better results. The position taken by the entering acyl group does not vary with the catalyst used. Three methods were employed to establish the orientation of the product :—(*a*) determination of the m.p. and that of a derivative, *e.g.* (V) ; (*b*) relation of the product to a compound of known structure, *e.g.* (XI) ; (*c*) direct comparison of the aluminium chloride and sulphuric acid products, *e.g.* (VIII). Features of interest in regard to the results are given below under the heading of the compound acylated.

Phloroglucinol trimethyl ether (I) (Fig. 1). The structure of the product (II) was confirmed by demethylation (yield 79%) to (III) using aluminium chloride in ether (see 4). Since phloroglucinol can be trimethylated through the tri-acetate in about 75% over-all yield (19 ; cf. 18) compounds (II) and (III) can now be obtained from phloroglucinol in over-all yields of about 75% and 60%, respectively. Application of the Hoesch method to (I) is not satisfactory for the production of (II) (see 8, 67). An alternative method of synthesising (III) which involves the preparation of phloracetophenone by the Hoesch method (28, 29, 30, 36, 60) and subsequent methylation to (III), (see 63), gives approximately the same over-all yield in fewer stages. It requires, however, a more elaborate technique, and the operations extend over a period of five days (29).

Compound (III) can also be prepared by application of the Hoesch method to phloroglucinol dimethyl ether, but the yield is unsatisfactory (8, 20, 55, 67). In connection with the syntheses of (II) and (III) it is interesting to note that Hoesch (36) in the introduction to his classical paper on the ketimine synthesis for hydroxyacetophenones which bears his name, states that he was led to devise the synthesis because of the need for a reliable " mild " method for introducing the acetyl group into the active phloroglucinol nucleus ; derivatives of phloracetophenone are of importance owing to their occurrence in flavones and related natural products. As is well known aluminium chloride, ferric chloride, and zinc chloride, when used as catalysts give poor results in the acylation of phloroglucinol (36, 51, 61, 68).

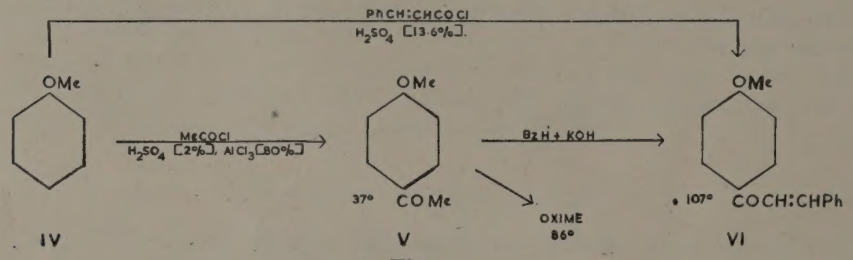


Fig. 2.

Anisole (IV) (Fig. 2). Much formation of resin occurred using acetyl chloride and sulphuric acid ; a somewhat similar result is obtained with acetic anhydride and sulphuric acid (for references see 64), though Schneider and Meyer (66) obtained (V) from (IV) in over 30% yield using acetic anhydride and sulphuric acid. Cinnamoyl chloride gives with (IV) and sulphuric acid a better yield of ketone than does acetyl chloride. The structure of (V) was confirmed by synthesis, using aluminium chloride (71), of an authentic specimen, and by preparation of the oxime. Compound (VI) was then oriented by synthesis from (V) by chalkone condensation with benzaldehyde.

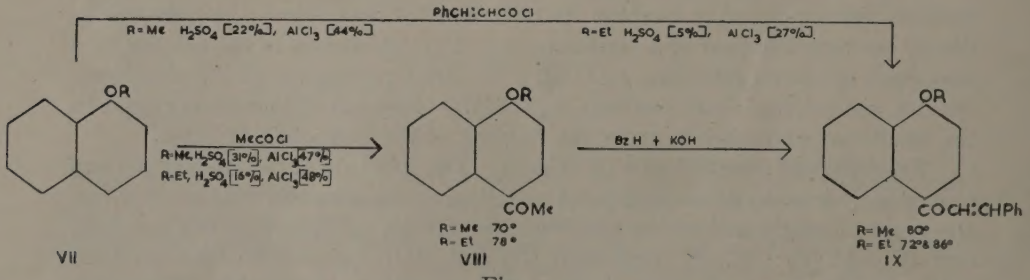


Fig. 3.

α-Naphthyl ethers (VII) (Fig. 3). The structures of the sulphuric acid-acyl chloride products (VIII ; IX) which were obtained in poor to moderate yields follow from their identity with the Friedel-Crafts products (25 ; 70). The sulphuric acid-acetic anhydride product from (VII ; R=Me) is also (VIII ; R=Me) (65). *Styryl 4-methoxy-1-naphthyl ketone* (IX ; R=Me) does not seem hitherto to have been prepared. Styryl 4-ethoxy-1-naphthyl ketone (IX ; R=Et) was found to be dimorphic (for details see *Experimental*).

OR
R = Me 72°
R = Et 37°
X
R=Me, H_2SO_4 (33%), $AlCl_3$ (20%)
R=Et, H_2SO_4 (40%)
PhCH:CHCOCl
MeCOCl
R=Me, H_2SO_4 (64%)
R=Et, H_2SO_4 (49%), $AlCl_3$ (51%),
$ZnCl_2$ (21%)
COMe OR
R = Me 60°
R = Et 61°
XI
COCH:CHPh OR
R = Me 140°
R = Et 87°
XII
RH + KOH
R=Et 48% w/v HBr/HAc (27%)
Methylation or Ethylation
OH
120°
XVI
COMe OH
64°
XV
OCOMe
70°
XIV
FRIES
$AlCl_3$
OMe COMe
48°
XVII
RH + KOH
OMe COCH:CHPh
121°
XVIII
R = Me
ZnCl2 in NO2 PhCl (5%)
OMe
107°
XIII
MeOC
p-Nitrophenylhydrazone
239–40°
RH + KOH
OMe
121°
XIX
PhHC:HCOC

Fig. 4.

β-Naphthyl methyl ether (X ; R=Me) *and acetyl chloride* (Fig. 4). The structure of the product (XI ; R=Me) was confirmed by a mixed m.p. determination with an authentic sample obtained by methylation (22) of 2-hydroxy-1-acetonaphthone (XV), which itself was prepared by transformation of β-naphthyl acetate (XIV) by the method of Fries, who proved his product (XV) to be the 1 : 2—compound (22). In agreement with Witt and Braun (78), however, Fries (22) first regarded the Friedel-Crafts product from (X ; R=Me) and acetyl chloride as (XVII). Later (23) he showed that, as suggested by Rousset (62), the Friedel-Crafts product had also the structure (XI ; R=Me) ; this compound was also obtained from (X ; R=Me) using sulphuric acid-acetic anhydride (65). The incorrect formulation of (XI) by Witt and Braun (78) and initially by Fries (22) misled Dilthey and Lipps (14) and Dimroth (15).

Compound (XVII) was itself first prepared by Fries and Schimmelschmidt (23) from 2-methoxy-3-naphthoic acid, and later by Wahl (74, 75). Galle (24) claimed that (X ; R=Me) with acetyl chloride and titanium tetrachloride gave (XVII) and not the expected (XI ; R=Me). The m.p. he quotes for his product (57·5—58) is that of (XI, R=Me) and not that of (XVII), which is 48° (23).

β-Naphthyl methyl ether (X ; R=Me) *and cinnamoyl chloride* (Fig. 4). The structure of the sulphuric acid-cinnamoyl chloride product (XII ; R=Me) was established by its identity (mixed m.p.) with the benzaldehyde chalkone prepared from (XI : R=Me) as described by Fries and Schimmelschmidt (23). Monti (49) stated that the action of cinnamoyl chloride on (X ; R=Me) in presence of aluminium chloride gave styryl 2-methoxy-3-naphthyl ketone (XVIII). The improbability of this result was pointed out by Motwani, Bodani and Wheeler (50) ; repetition of the work now shows that (XII ; R=Me) is actually obtained. Further, synthesis of (XVIII) by chalkone condensation of benzaldehyde with (XVII) as described by Fries and Schimmelschmidt (23), whose work was overlooked by Monti, has confirmed that (XVIII) is not the product of Monti's reaction.

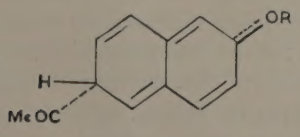
Compound (XII ; R=Me) was also prepared by Koelsch and Anthes (42) from (X ; R=Me), cinnamic acid and phosphorus pentachloride, followed by treatment of the mixture with aluminium chloride ; they established the structure of the product by showing it to be identical with the benzaldehyde chalkone from (XI ; R=Me). These authors do not refer to the work of Fries and Schimmelschmidt (23), nor, though they cite Monti (49), do they seem to have been aware of her incorrect formulation of (XII ; R=Me).

β-Naphthyl ethyl ether (X ; R=Et) (Fig. 4). β-Naphthyl ethyl ether gave with sulphuric acid and the acid chlorides employed results similar to those obtained with the methyl ether. The structure of (XI ; R=Et) was established by its identity with the ethylation product of (XV). Attempts to de-ethylate (XI ; R=Et) to (XV) with hydrogen bromide in glacial acetic acid were unsuccessful ; β-naphthol (XVI) was, unexpectedly, the only product. Fries and Schimmelschmidt (23) corrected Witt and Braun (78), who thought (XI ; R=Et) was the 2 : 3-derivative. As

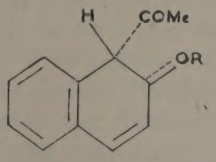
pointed out above, these workers held the same incorrect view in regard to (X ; R=Me). Compound (XII ; R=Et) as prepared by the sulphuric acid method was oriented by its formation from (XI ; R=Et) by the chalkone reaction with benzaldehyde.

Compound (XII ; R=Et) is of interest in that it was first prepared by Dilthey and Lipps (14) by condensation of benzaldehyde with a compound which they thought was (XVII) but was in fact (XI ; R=Et). They assigned the structure (XVII) to the product they obtained from acetyl chloride, aluminium chloride, and what they thought was (X ; R=Me) on the basis of the then current views of Fries (22), which, as stated above, were incorrect. When Fries and Schimmelschmidt (23) synthesized (XVII) they re-examined the work of Dilthey and Lipps (14), and showed that these chemists had in hand, not (XI ; R=Me) but (XI ; R=Et) ; the m.ps. of these compounds are both close to 60°.

Fries and Schimmelschmidt (23) could offer no adequate explanation for Dilthey and Lipps' error, which extended to a number of derivatives. While the present work was in progress, however, a commercial sample of β-naphthyl methyl ether, which was labelled " nerolin," and of which a crystal had the correct m.p. (72°) for the methyl ether, gave anomalous results, finally yielding (XII ; R=Et). Re-examination of the batch showed that it consisted of a coarse mixture of β-naphthyl methyl and ethyl ethers. It seems that commercially both ethers are included in the term " nerolin," (Nerolin I and II). Dilthey and Lipps' results may have been due to the use of such a mixture for the methyl ether.



XX



XXI

Fig. 5.

As it was required for reference, 2-methoxy-6-acetonaphthone (XIII ; R=Me) was prepared by the action of acetyl chloride on (X, R=Me) in presence of zinc chloride and nitrobenzene (11, 23, 32, 59). It readily yielded the corresponding chalkone, *styryl 2-methoxy-6-naphthyl ketone* (XIX). Using the same technique with (X ; R=Et) there was obtained (XI ; R=Et) and not the expected 2 : 6-derivative. Presumably the transition compounds (XX) and (XXI) (see Fig. 5) which may be regarded as intermediate in 6- and 1- substitution, respectively, vary in stability with R (see 76, 77), so that nitrobenzene does not promote (XX) when R is Et. (In regard to the effect of solvents on the course of the Friedel-Crafts reaction see (15A)).

No useful result was obtained with sulphuric acid, acetyl chloride, and *m*- or *p*-dimethoxybenzene.

Experimental.

Phloracetophenone Derivatives (*Fig* 1).

Phloracetophenone trimethyl ether (II). A mixture of phloroglucinol trimethyl ether (I), (10 g.), acetyl chloride (10 ml. ; 2.3 mol.), and ethyl ether (10 ml.), was treated dropwise (shaking) with concentrated sulphuric acid (5 ml. ; 1.6 mol.), and water (200 ml.) was added after 12 hrs. The precipitated solid (12.5 g. ; 100% yield) had m.p. 97—9° ; lit. (18, 21, 44, 73) 97-102°. The trimethyl ether (I) was obtained from phloroglucinol through the tri-acetate by the method of Freudenberg (19) in the yield shown in Fig. 1.

2-*Hydroxy*-4:6-*dimethoxyacetophenone* (III). Phloracetophenone trimethyl ether (II) (25 g.) was added to an ethereal solution of anhydrous aluminium chloride (160 g.) prepared by slow addition of dry ether (600 ml.) to the chloride in a reflux apparatus (ice-cooling ; calcium chloride guard). The mixture was heated under reflux for 12 hrs., and poured into excess of hydrochloric acid (10%) containing ice. The ethereal extract was washed with water, and extracted with aqueous sodium hydroxide (2%). The required product was precipitated from the alkaline extract by acidification ; yield 18.5 g. (79%) ; m.p. 81° ; lit. (8, 63, 73) 80-3° ; (21) 85-8°.

Condensations with Anisole. (*Fig.* 2).

p-*Methoxyacetophenone* (V). A mixture of anisole (IV) (20 g.) and acetyl chloride (16 ml. ; *ca* 1 mol.), which had been treated dropwise with concentrated sulphuric acid until no further action occurred (*ca.* 7 g. ; 0.4 mol.), was heated at 40° under a reflux for 0.5 hr. When cool the resulting mixture was washed with water and with aqueous sodium hydroxide (5%) ; a red amorphous solid separated when the alkali was added. The ethereal extract of the mixture of alkali and product was washed with water and dried (anhydrous sodium sulphate) and the solvent was evaporated. The residue when distilled under reduced pressure (*ca.* 10^{-3} mm.) gave mainly resin and a small yield (0.5 g. ; 2%) of *p*-methoxyacetophenone ; m.p. 37° ; lit. (25, 53, 71) 36-9°. The yield with aluminium chloride amounts to 75–86% (71 ; cf. 2). The oxime had m.p. (light petroleum) 86° ; lit. (3) 86–7°.

p-*Methoxyphenyl styryl ketone* (VI). A mixture of anisole (IV) (5 g.) and cinnamoyl chloride (8 g. ; 1 mol.) was treated with concentrated sulphuric acid (0.1 ml.) at 130°. Hydrogen chloride was evolved, and the temperature of the mixture was allowed to come to 160° at which point it was kept for 0.5 hr. When cool the product was extracted with chloroform, and the extract was washed with water, aqueous sodium carbonate (10%), again with water, and dried (anhydrous sodium sulphate). The solvent was evaporated, and the residue distilled at *ca.* 10^{-4} mm. as read on a McLeod guage. The solid distillate was sublimed at 10^{-5} mm. ; the sublimate had m.p. (alcohol) 105-7° ; lit. (69, 70) 105-7°. Yield 1.5 g. (13.6%). The product was not depressed in m.p. when mixed with the chalkone from (V) and benzaldehyde. (See 69).

Condensations with α-Naphthyl Ethers. (*Fig.* 3).

4-*Methoxy*-1-*acetonaphthone* (VIII ; R=Me). A mixture of α-naphthyl methyl ether (VII ; R=Me) (5 g.) and acetyl chloride (3 ml. ; 1.2 mol.) was treated under reflux with sulphuric acid (0.2 ml.) at 40°, and maintained at that temperature for 0.5 hr. The residue obtained by chloroform extraction and further treatment as in the preparation of (VI) was distilled at 0.4 mm. ; the distillate had m.p. (light petroleum) 70° ; lit. (12, 25, 54, 65) 70–2°. Yield 2 g. (31%). The m.p. was not depressed by admixture with an authentic specimen prepared (yield 47%) using aluminium chloride as a catalyst (25, 78).

Styryl 4-*methoxy*-1-*naphthyl ketone* (IX; R=Me). *Preparation using sulphuric acid.* A mixture of (VII ; R=Me) (5 g.) and cinnamoyl chloride (5 g. ; 1 mol.) was treated with sulphuric acid (0.2 ml.) at 100°. The mixture was kept at 130° for 0.5 hr., and worked up as in the preparation of (VI). The red semi-solid wax obtained by distillation at 4 x 10^{-4} mm. separated from ligroin-absolute alcohol in yellow crystals (needles) with m.p. 79–80° ; yield 2 g. (22%). (Found : C, 83.6 : H, 5.6. $C_{20}H_{16}O_2$ requires C, 83.3 ; H, 5.6%).

Preparation of (IX ; R=Me) *using aluminium chloride.* Anhydrous aluminium chloride (4 g. ; *ca* 1.6 mol.) was added in small lots to a mixture of α-naphthyl methyl ether (3 g.), cinnamoyl chloride (3 g. ; 1 mol.), and carbon disulphide (10 ml.), which was cooled in ice-water, and the whole was then heated under reflux at 100° for 1 hr., cooled, and treated with ice and hydrochloric acid (10%). The ethereal extract of the product was washed with aqueous sodium hydroxide (5%) and with water, and dried (anhydrous sodium sulphate). The distillate (at 0.04 mm.) from the residue obtained on evaporation, of the solvent was crystallized from ligroin-absolute alcohol ; m.p. 79–80° ; yield 4 g. (44%).

Preparation of (IX ; R=Me) *by condensation of benzaldehyde with* (VIII ; R=Me). A mixture of (VIII ; R=Me) (0.5 g.), benzaldehyde (0.2 ml. ; *ca.* 1 mol.), and alcoholic potassium hydroxide (20% ; 2 ml.), was shaken over-night, and diluted with water to precipitate the crude product (yield 87%), which after recrystallization from ligroin-absolute alcohol had m.p. 79–80°.

The structure of (IX ; R=Me) was confirmed by the fact that the mixed m.p. of the products from the three methods of preparation showed no depression.

4-*Ethoxy*-1-*acetonaphthone* (VIII ; R=Et) was prepared using sulphuric acid in the same manner as (VIII ; R=Me) ; yield 16% ; m.p. 78° ; lit. (25,41,78) 77–9° The m.p. was not depressed by admixture with an authentic specimen prepared (yield 48%) using aluminium chloride (25, 41, 78).

Styryl 4-*ethoxy*-1-*naphthyl ketone* (IX ; R=Et) was prepared using sulphuric acid in the same manner as (IX ; R=Me) ; yield 5%. The m.p. of the product was not depressed by admixture with an authentic sample prepared (see 70), using aluminium chloride (yield 27%), or by chalkone condensation (see 14) of (VIII ; R=Et) with benzaldehyde. (Found : C, 83.1 ; H, 5.9. Calc. for $C_{21}H_{18}O_2$; C, 83.5 ; H, 6.0%).

The m.p. of the product obtained by the three methods mentioned above was 72–4° Stockhausen and Gattermann (70) and Dilthey and Lipps (14) give m.p. 85–6° ; Dilthey and Lipps, who claimed the compound as new, mention that they obtained yellow needles except in one instance when almost colourless plates were produced, which formed the yellow needles on recrystallisation. The product, from all preparations made in the course of this work was a mixture of the two forms with m.p. 72–4°. By rapid cooling of an alcoholic solution the colourless plates with m.p. 72° were obtained. Repeated (8 times) recrystallization from alcohol increased the proporion of yellow needles, the m.p. eventually reaching 77–9°. When the mixture was shaken for 48 hours in contact with alcohol at room temperature the m.p. rose to 83-84.5°. This product on recrystallization (twice) from alcohol formed pale yellow needles with m.p. 85.5–86.5°.

Condensations with β-Naphthyl Methyl Ether (*Fig.* 4).

2-*Methoxy*-1-*acetonaphthone* (XI ; R=Me). A mixture of β-naphthyl methyl ether (X ; R=Me) (5 g.) and acetyl chloride (3 ml. ; 1.2 mol.) was treated at 70° with concentrated sulphuric acid (4 drops), and the mixture was heated under reflux until the temperature of the vapour reached 110° (0.5 hr.). The residue obtained by chloroform extraction of the product, and treatment as in the preparation of (VI), gave a fraction with b.p. 82–88/10^{-4} mm. and m.p. (ligroin) 60° ; lit. (22, 25, 78) 57–9°; yield 1 g.; (16%). The m.p. was not depressed by admixture with an authentic sample of 2-methoxy-1-acetonaphthone prepared from (XIV) through (XV) (22).

Styryl 2-methoxy-1-*naphthyl ketone* (XII ; R=Me). A mixture of β-naphthyl methyl ether (5 g.) and cinnamoyl chloride (5 g. ; 1 mol.) which had been treated at 130° with concentrated sulphuric acid (1 drop) was kept for 0.5 hr. at that temperature. A vigorous evolution of hydrogen chloride occurred. The solution of the cooled mixture in chloroform after it had been treated as described in the preparation of (VI) gave, on removal of the solvent and subsequent recrystallization, a solid with m.p. (alcohol) 140° ; lit. (23) 139° ; yield 3 g. (33%). The m.p. was not depressed (*a*) by admixture with an authentic sample prepared from (XI ; R=Me) by condensation with benzaldehyde, as described by Fries and Schimmelschmidt (23) ; (*b*) when mixed with the product obtained from β-naphthyl methyl ether, cinnamoyl chloride and aluminium chloride, using the method described by Monti (49) ; yield 20%. Compound (XVIII) when prepared by the method of Fries and Schimmelschmidt (23) had m.p. 123°, lit. (23) 121°, strongly depressed by admixture with Monti's compound.

Condensations with β-Naphthyl Ethyl Ether (*Fig.* 4).

2-*Ethoxy*-1-*acetonaphthone* (XI ; R=Et). A mixture of β-naphthyl ethyl ether (X ; R=Et) (5 g.) and acetyl chloride (5 ml. ; 2.2 mol.) was treated at 40° in a reflux apparatus with concentrated sulphuric acid (0.1 ml.). The temperature was maintained for 1 hr., and the product was then treated with water. The

crystalline distillate (at 10^{-3} mm.) from the residue from the alkali-washed and dried (anhydrous sodium sulphate) ethereal extract (see above in the preparation of (V)) had m.p. (alcohol) 61°; lit. (23, 25) 61–3°; yield 0.85 g. (14%). The m.p, was not depressed by admixture with an authentic sample prepared (yield 51%) using aluminium chloride (25) or from (XV) by ethylation.

Preparation of (XI; R=Et) *by ethylation of* (XV). A mixture of (XV) (0.5 g.), metallic sodium (0.1 g.; 1.6 atom), ethyl iodide (0.5 g.; 1.2 mol.) and ethyl alcohol (5 ml.) was heated under reflux for 2 hrs. and poured into water. The ethereal extract of the aqueous mixture was washed with water, and dried over anhydrous sodium sulphate. The residue obtained on evaporation of the solvent had m.p. (alcohol-light petroleum) 59–61°; yield 0.42 g. (73%). (cf. 23).

Preparation of (XI; R=Et) *using zinc chloride as catalyst and nitrobenzene as solvent.* A mixture of β-naphthyl ethyl ether (15 g.), acetyl chloride (8 ml.; 1.2 mol.), zinc chloride (13 g.; 1.1 mol.), and nitrobenzene (70 ml.), was kept at room temperature for 48 hrs., treated with hydrochloric acid (10%), and steam distilled. The ethereal extract of the residue was washed with water and dried (anhydrous sodium sulphate), and the solvent evaporated. The solid distillate (at 10^{-3} mm.) obtained from the residue left on removal of the solvent, had m.p. (ligroin) 61°, not depressed by admixture with the product of the sulphuric acid condensation. Yield 4 g.; (21%).

De-ethylation of (XI; R=Et). A mixture of (XI; R=Et) (1 pt.), glacial acetic acid (8 pts.) and hydrobromic acid (4 pts. of 48% acid) which had been kept overnight, was heated under reflux for 4 hrs. and poured into water. The ethereal extract of the product was washed with aqueous sodium hydrogen carbonate (5%) and with water and extracted with aqueous sodium hydroxide (5%). β-naphthol (XVI) m.p. (alcohol), and mixed m.p. with authentic specimen, 120°, separated on acidification of the alkaline extract (yield 97%).

Styryl 2-ethoxy-1-naphthyl ketone (XII; R=Et). A mixture of β-naphthyl ethyl ether (5 g.), cinnamoyl chloride (5 g.; 1 mol.) and concentrated sulphuric acid (0·1 ml.) which had been heated at 100° for 1 hr. was cooled, diluted with water and the product extracted with ether. The extract was treated as described in the preparation of (V). The solid distillate at 10^{-3} mm. from the residue obtained on removal of the solvent had m.p. (alcohol) 87°; lit. (14, 23) 87-90°; yield 3.5 (40%). The m.p. was not depressed by admixture with the product obtained by condensation of (XI; R=Et) with benzaldehyde (23; cf.14).

Styryl 2-methoxy-6-naphthyl ketone (XIX) (Fig. 4). 2-Methoxy-6-acetonaphthone (XIII) was prepared by the method of Desai and Waravdekar (11); yield 5%. The m.p. of the product (107°) and that of the *p*-nitrophenylhydrazone (230-40°) were in agreement with the figures given by these authors. Condensation with benzaldehyde by the usual technique (see 23) gave the *styryl ketone* (XIX) as needles with m.p. (alcohol) 121°; yield 90%. (Found: C, 83.0; H, 5.6. $C_{20}H_{16}O_2$ requires C, 83.3; H, 5.6%).

SUMMARY.

Sulphuric acid has been found to be an effective catalyst (yield 100%) for the introduction of an acetyl group into the activated nucleus of phloroglucinol trimethyl ether. With less activated nuclei, yields of the required derivatives are, on the whole, low. The point of entrance of the acyl group is the same as that obtained with aluminium chloride.

In the course of the work opportunity has been taken to clear up some anomalous results in the chemistry of the alkoxynaphthyl ketones.

One of us (N.V.N.) acknowledges with thanks the award of a maintenance allowance by the Minister for Education. The authors are indebted to Imperial Chemical Industries, Ltd. for a grant towards the cost of the work.

Analyses by Drs. Weiler and Strauss (Oxford).

Department of Chemistry,
University College,
Dublin.

REFERENCES.

1. ALGAR, J., *Private communication.*
2. ADAMS, R. and NOLLER, C. R., *Organic Syntheses.* Chapman and Hall (London, 1941), **1**, 111.
3. AUWERS, K., LECHNER, M., and BUNDESMANN, H., *Ber.*, 1925, **58**, 51.
4. BAKER, W., *J. Chem. Soc.*, 1941, 662.
5. *Beilstein*, VIII. Spt., 688.
6. BRAND, K., and COLLISCHONN, H., *J. pr. Chem.*, 1922, **103**, 329.
7. CALLOWAY, N. O., *Chem. Rev.*, 1935, **17**, 327.
8. CANTER, F. W., CURD, F. H., and ROBERTSON, A., *J. Chem. Soc.*, 1931, 1245.
9. COX, E. H., *Rec. trav. chim.*, 1931, **50**, 848.
10. CULLINANE, N. M., ALGAR, J., and RYAN, H., *Proc. Roy. Dublin Soc.*, 1929, **19**, 77.
11. DESAI, R. D., and WARAVEDEKAR, W. S., *Proc. Indian Acad. Sci.*, 1946, **24**A, 382.
12. DEY, B. B., and RAJAGOPALAN, S., *Arch. Pharm.*, 1939, **277**, 377.
13. DILTHEY, W., *Ber.*, 1938, **71**, 1350.
14. DILTHEY, W., and LIPPS, G., *Ber.*, 1923, **56**, 2443.
15. DIMROTH, O., *Annalen*, 1926, **446**, 116.
15A. EITEL, A. and FIALLA, R., *Monatsh.*, 1948, **79**, 112.
16. FAIRBROTHER, F., *J. Chem. Soc.*, 1937, 503.
17. FAIRBROTHER, F., *Trans. Faraday Soc.*, 1941, **37**, 763.
18. FREUDENBERG, K., *Ber.*, 1920, **53**, 1416.
19. FREUDENBERG, K., *Annalen*, 1923, **433**, 230.

20. FREUDENBERG, K., FIKENTSCHER, H., and WENNER, W., *Annalen*, 1925, **442**, 309.
21. FRIEDLÄNDER, P., and SCHNELL, L. C., *Ber.*, 1897, **30**, 2150.
22. FRIES, K., *Ber.*, 1921, **44**, 709.
23. FRIES, K., and SCHIMMELSCHMIDT, K., *Ber.*, 1925, **58**, 2835.
24. GALLE, R. R., *J. Gen. Chem.* (*U.S.S.R.*), 1938, **8**, 402; *Chem. Abs.*, 1938, **32**, 7910.
25. GATTERMANN, L., EHRHARDT, R., and MAISCH, H., *Ber.*, 1890, **23**, 1199.
26. GÖSCHKE, A., and TAMBOR, J., *Ber.*, 1912, **45**, 1237.
27. GOTTESMANN, E., *Ber.*, 1933, **66**, 1168.
28. GULATI, K. C., SETH, S. R., and VENKATARAMAN, K., *J. Chem. Soc.*, 1934, 1765.
29. GULATI, K. C., SETH, S. R., and VENKATARAMAN, K., *Organic Syntheses*. Chapman and Hall (London, 1943), **2**, 522.
30. GULATI, K. C., and VENKATARAMAN, K., *J. Chem. Soc.*, 1936, 267.
31. HARTOUGH, H. D., and KOSAK, A. I., *J. Amer. Chem. Soc.*, 1947, **69**, 3093.
32. HAWORTH, R. D., and SHELDRICK, G., *J. Chem. Soc.*, 1934, 864.
33. HELLER, C., *Ber.*, 1909, **42**, 2738.
34. HELLER, G., *Ber.*, 1912, **45**, 418.
35. HELLER, G., *Ber.*, 1915, **48**, 1286.
36. HOESCH, K., *Ber.*, 1915, **48**, 1122.
37. HOWELLS, H. P., and LITTLE, J. G., *J. Amer. Chem. Soc.*, 1932, **54**, 2451.
38. ISRAELSTAM, S. S., *J. S. African Chem. Inst.*, 1943, **26**, 49.
39. ISRAELSTAM, S. S., *J. S. African Chem. Inst.*, 1944, **27**, 15.
40. ISRAELSTAM, S. S., and STEPHEN, H., *J. S. African Chem. Inst.*, 1943, **26**, 41.
41. KAMM, O., MCCLUGAGE, H. B., and LANDSTROM, A. W., *J. Amer. Chem. Soc.*, 1917, **39**, 1242.
42. KOELSCH, C. F., and ANTHES, J. A., *J. Org. Chem.*, 1941, **6**, 558.
43. KOSAK, A. I., and HARTOUGH, H. D., *J. Amer. Soc.*, 1947, **69**, 3144.
44. KOSTANECKI, S., and TAMBOR, J., *Ber.*, 1899, **32**, 2260.
45. LEUCHS, H., and SPERLING, R., *Ber.*, **48**, 135.
46. LINSTEAD, R. P., *Annual Repts. Chem. Soc.*, 1937, **34**, 251.
47. LUDOR, W. F., and ZUFFANTI, S., *Electronic Theory of Acids and Bases*. Chapman and Hall (London, 1946).
48. MALIN, G., *Annalen*, 1866, **138**, 78.
49. MONTI, L., *Gazzetta*, 1930, **60**, 43.
50. MOTWANI, D. C., BODANI, V. V., and WHEELER, T. S., *Current Sci.*, 1938, **6**, 604.
51. NENCKI, M., *Ber.*, 1899, **32**, 2414.
52. NENCKI, M., and SIEBER, N., *J. pr. Chem.*, 1881, **23**, 147.
53. NOLLER, C. R., and ADAMS, R., *J. Amer. Chem. Soc.*, 1924, **46**, 1889.
54. PFEIFFER, P., and HAACK, E., *Annalen*, 1928, **460**, 156.
55. PRATT, D. D., and ROBINSON, R., *J. Chem. Soc.*, 1924, **125**, 188.
56. PRICE, C. C., *Organic Reactions*. Chapman and Hall (London, 1947), **3**, 1.
57. PRICE, C. C., and MEISTER, M., *J. Amer. Chem. Soc.*, 1939, **61**, 1595.
58. PULLMAN, B., *Bull Soc., chim.*, 1948, **15**, 533.
59. ROBINSON, R., and RYDON, H. N., *J. Chem. Soc.*, 1939, 1394.

60. Robinson, R., and Venkataraman, K., *J. Chem. Soc.*, 1926, 2344.
61. Rosenmund, K. W., and Schultz, H., *Arch. Pharm.*, 1927, **265**, 308.
62. Rousset, L., *Bull. Soc. chim.*, 1897, **17**, 312.
63. Sastri, V. D. H., and Seshradi, T. R., *Proc. Indian Acad. Sci.*, 1946, **23**A, 262.
64. Schneider, W., and Gramms, G., *Ber.*, 1936, **69**, 2543.
65. Schneider, W., and Kunau, F., *Ber.*, 1921, **54**, 2302.
66. Schneider, W., and Meyer, H. F. W., *Ber.*, 1921, **54**, 1484.
67. Shinoda, J., *J. Pharm. Soc. Japan*, 1927, No. 548, 834; *Chem. Abs.*, 1928, **22**, 768.
68. Shriner, R. L., and Kleiderer, E. C., *J. Amer. Chem. Soc.*, 1929, **51**, 1267.
69. Staudinger, H., and Kon, N., *Annalen*, 1911, **384**, 123.
70. Stockhausen, F., and Gattermann, L., *Ber.*, 1892, **25**, 3538.
71. Straus, F., *Annalen*, 1910, **374**, 139.
72. Thomas, C. A., *Anhydrous Aluminium Chloride in Organic Syntheses.* Reinhold Publishing Corp. (New York, 1941), chapter 4.
73. Tutin, F., and Caton, F. W., *J. Chem. Soc.*, 1910, **97**, 2062.
74. Wahl, H., *Compt. rend.*, 1938, **206**, 521.
75. Wahl, H., and Fraemohs, J., *Compt. rend.*, 1947, **224**, 573.
76. Ward, E. R., *Chem. and Ind.*, 1948, 781.
77. Waters, W. A., *J. Chem. Soc.*, 1948, 727.
78. Witt, O. N., and Braun, O., *Ber.*, 1914, **47**, 3216.